

# Auxiliary liver transplantation for acute liver failure

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## Background

In patients with acute liver failure (ALF) who fulfil criteria, liver transplantation is the only effective treatment which can substitute metabolic and excretory function of the liver. Auxiliary liver transplantation was developed because a significant minority of patients with ALF who fulfil transplant criteria can have a complete morphological and functional recovery of their liver. The favourable outcome reported in European series using auxiliary partial orthotopic liver transplantation (APOLT), the greater experience as well as the lessons from split liver and from living related donors have revived interest in this approach. In selected patients aged <40 years without haemodynamic instability, the use of ABO-compatible, non-steatotic grafts harvested from young donors with normal liver function can restore liver function and prevent the occurrence of irreversible brain damage. In the

majority of cases the auxiliary graft is a right graft which is placed orthotopically after a right hepatectomy in the recipient. After standard immunosuppression, the recovery of the native liver is assessed by biopsies, hepatobiliary scintigraphy and computed tomography. When, on the basis of histological, scintigraphical and morphological data, there is evidence of sufficient regeneration of the native liver, immunosuppression can be discontinued progressively. Complete regeneration of the native liver can be observed in >50% of patients, who can be withdrawn from immunosuppression. Therefore the advantages of auxiliary transplantation seem to balance favourably with the potential inconvenience of this technique in selected patients.

## Keywords

ALF, APOLT

## Introduction

The main causes of acute liver failure (ALF) leading to consideration of patients for liver transplantation (LT) are viral hepatitis including B infection and drug- or toxin-induced hepatic injury including paracetamol overdose. In the majority of cases, patients who were previously healthy can recover without liver parenchymal sequelae. Severe forms progress to multisystem failure including cerebral oedema, which can cause death within a few hours or a few days. In this situation, LT is the only effective treatment that can substitute metabolic and excretory function of the liver. LT is indicated when severe encephalopathy (confusion or coma) is associated with an important decrease of the coagulation factors (factor V < 20%) [1]. Orthotopic liver transplantation (OLT) is an established treatment for ALF with 1-year patient survival rates of approximately 60–70% [2]. Nevertheless, a significant minority of patients with ALF who fulfil transplant criteria would have had complete morphological and functional recovery of their

liver if they had not undergone OLT [3]. These considerations have led to the concept of auxiliary liver transplantation, which does not exclude the potential for spontaneous regeneration of the native liver and eventual withdrawal of immunosuppressive drugs [4–7]. Auxiliary liver transplantation consists of implanting a healthy liver graft placed either heterotopically or orthotopically while leaving all or part of the native liver. Early experience with heterotopic placement of the graft below the native liver has been disappointing with a high rate of technical failure, probably due to inadequate portal perfusion of the graft and insufficient drainage of hepatic blood flow in an area of low pressure (Figure 1) [4, 8, 9]. The favourable outcome reported in a European series using auxiliary partial orthotopic liver transplantation (APOLT), the greater experience as well as the lessons from split liver and from living related donors have revived interest in this approach [10–12]. The aim of this paper is to summarize our current selection of patients, technical procedure and the postoperative management, focusing on the withdrawal of immunosuppression.

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## Technical procedure

APOLT requires that both the graft and the recipient's liver are reduced. Although, early in our experience, we have used full-size grafts in four recipients, this is associated with a high incidence of vascular complications owing to difficulties in correctly orienting the graft and compression by the abdominal wall and we no longer use or advocate this technique [13]. Size reductions are performed on opposite sites (removing left segments of the recipient's liver and right segments of the graft or the other way round) so that after transplantation, the patient has an approximately normal overall liver volume. Technically the surgical team has the choice of the topography and extent of the resections provided that an anatomical transection of the liver is performed. In practice, this is governed by the size of the graft and by the severity of the recipient's encephalopathy. Unless we use a graft from a living donor, an important issue is whether the part of the liver not used for auxiliary liver transplantation is discarded or used in another patient as part of a split transplantation. Owing to the relative scarcity of donor organs the latter option is obviously the best. However, one should be aware that the splitting procedure increases the duration of the back table procedure (this may prove detrimental to the recipient if they have severe encephalopathy), and decreases the size and the length of both portal and arterial vessels. In fact, partial grafting in auxiliary liver transplantation primarily aims to obtain a smaller graft that can fit the limited space available in the abdominal cavity. If this

also allows another patient to be transplanted it is an ideal goal; however, that should not put the recipient of the APOLT at increased risk.

The surgical procedure consists of three main steps, as described below.

## Recipient procedure

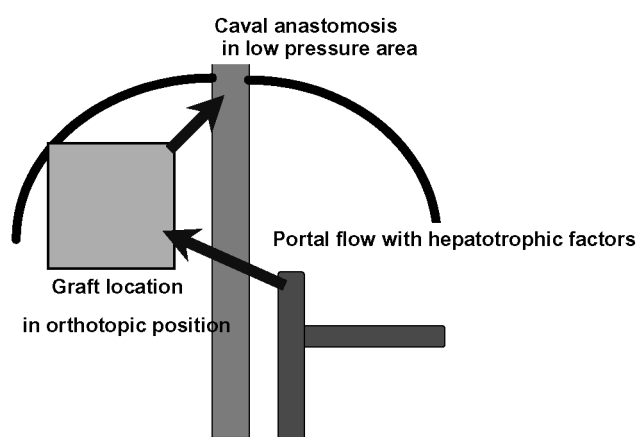
In the recipient procedure, a frozen section biopsy of the native liver is usually sampled to assess the absence of fibrosis (that would otherwise suggest that poor regeneration of the native liver is expected) and the presence of viable hepatocytes. A right or a left hepatectomy of the native liver is performed in order to prepare a space large enough to accept a right or left liver graft, respectively. Right hepatectomies consist of resecting segments 5–8 (according to Couinaud's classification), while left hepatectomies consist of resecting the left lobe (segments 2 and 3) or the left liver including the Spiegel lobe. Although the parenchymal transection step tends to be easier in patients with fulminant liver failure because the liver is usually atrophic, resection can be performed under intermittent clamping. Because the resistance in the native liver is usually greater (due to extensive necrosis) than in the graft, no attempt is initially made to reduce portal flow.

## Donor procedure

Meanwhile, another team reduces the donor liver to a size compatible with its implantation beside the partially resected native liver. Two types of auxiliary grafts can be used to perform APOLT: a right liver (segments 5–8) or a left liver (segments 1–4). It is possible to use a right graft from a living donor.

## Orthotopic donor liver implantation

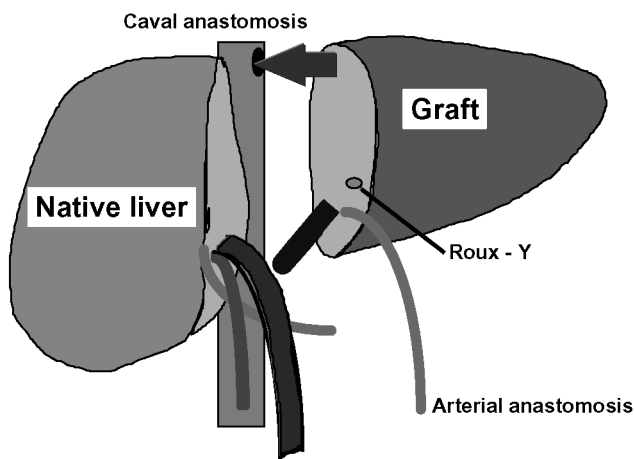
In the third step in the recipient procedure, the donor liver is implanted orthotopically. The right graft is placed in the right hypochondrium so that both cut surfaces of the graft and of the native liver are face-to-face (Figure 2). The graft is slightly rolled to the right to allow completion of an end-to-side caval anastomosis between the suprahepatic stump of the graft's inferior vena cava (IVC) and the recipient's vena cava. The right side of the recipient's portal vein is clamped laterally just above the head of the pancreas and opened. An end-to-side is performed between the graft's and the recipient's portal veins, using running sutures of the posterior wall and



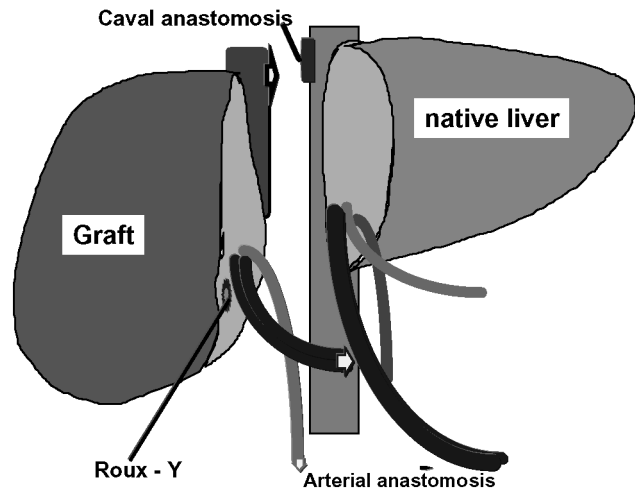
**Figure 1.** Prerequisite for functional liver graft showed that the graft should be placed orthotopically.

interrupted sutures of the anterior wall of 5/0 polypropylene. The graft is subsequently revascularised and the cut surface of the graft is explored to ensure that no haemorrhage is present. The graft's coeliac axis is anastomosed end-to-side to the recipient's splenic artery or infrarenal aorta. Bile flow is restored through a Roux-en-Y hepaticojejunostomy. Intra-operative ultrasound is mandatory to assess the patency of all vascular anastomoses. The right subphrenic space is drained. A primary abdominal closure is almost always possible. Should this result in a compression of the graft, the skin only is closed after extensive undermining on an absorbable mesh sutured to the musculofascial walls, full abdominal closure being performed some days or weeks later. We usually retain the drain placed in the recipient's cystic duct, to allow for monitoring of the native liver's bile and clearance function.

The left graft is put in the subphrenic space so that both cut surfaces of the graft and of the native liver are face-to-face (Figure 3). The graft is slightly rolled to the left to allow completion of an end-to-side caval anastomosis between the suprahepatic stump of the graft IVC and the left side of the recipient IVC. The graft's portal vein is anastomosed end-to-side by continuous running suture of the posterior wall and interrupted sutures of the anterior wall using 5/0 polypropylene. The graft is subsequently revascularised. Arterial and biliary reconstructions are performed as described for right grafts. One should be aware that the risk of parenchymal or vascular compression at the time of abdominal closure is greater



**Figure 2.** Auxiliary partial liver transplantation using left graft. In order to increase the space avoiding graft compression, resection in the recipient included segments 1–3.



**Figure 3.** Auxiliary partial liver transplantation using right graft.

with these left grafts. Intra-operative Doppler ultrasound is mandatory to ensure that blood flow in the arterial, portal and hepatic branches is normal.

### Postoperative management of immunosuppression

Conventional immunosuppression is started peroperatively. In patients transplanted with fulminant hepatitis B, a 14-day course of intravenous gancyclovir (5 mg/kg twice daily) and a 6-day course of intravenous anti-HBs Ig (10000 IU daily) are administered. Monitoring includes hepatobiliary scintigraphy with  $^{99m}\text{Tc}$ -trimethyl-Br-IDA tracer, computed tomography (CT) and, when necessary, transvenous biopsy or ultrasound-guided percutaneous biopsy.

When, on the basis of histological, scintigraphical and morphological data, there is evidence of sufficient regeneration of the native liver, immunosuppression can be discontinued according to two different options. The first option consists of abrupt discontinuation of all immunosuppressive agents, which is likely to be followed rapidly by severe and symptomatic rejection requiring surgical removal of the graft. The second option consists of progressive tapering of immunosuppression with the aim of inducing a slowly progressing chronic rejection with subsequent atrophy of the graft. According to our experience we suggest that progressive tapering of immunosuppression might be preferred to abrupt discontinuation [12].

## Patient selection

Severe forms of ALF progress to multisystem failure including cerebral oedema, which can cause death within a few hours or a few days. In this situation, LT is the only effective treatment that can substitute metabolic and excretory function of the liver. LT is indicated according to clinical and biological parameters known as the Clichy-King's College criteria [14, 15]. These include the aetiology of liver injury, the severity of the encephalopathy, the age of the patient, the factor V plasma level, the serum creatinine level and the pH. However, this prediction is not perfect and it is usually agreed that almost 20% of patients transplanted with these criteria would have survived without transplantation. This is obviously the first group of patients in whom auxiliary liver transplantation is most advantageous. However, because recipients of auxiliary partial liver grafts are undoubtedly at higher risk of early post-operative complications than recipients of an OLT, we believe that this procedure should not be performed earlier than standard OLT (i.e. should be indicated using the same criteria as those in use for conventional OLT).

Another group of patients in whom auxiliary liver transplantation will also prove useful are those patients in whom liver regeneration will occur but is delayed.

Previous results strongly suggest that regeneration is more likely to occur in those with a short interval between jaundice and encephalopathy [10–12, 16, 17]. Patients with hepatitis B belong to the group of acute liver diseases comprising fulminant hepatitis A and paracetamol overdose for which liver function is likely to return to normal after auxiliary transplantation [7, 10, 12, 18]. It is noteworthy that we have recently shown that in patients with HBV-related fulminant liver failure, there was a frequent disappearance of viral infection [12].

In patients with ALF, the first goal of liver transplantation is to restore liver function as soon as possible in order to reverse brain oedema and to prevent the occurrence of irreversible brain damage. Auxiliary liver transplantation will allow these patients to safely await regeneration and avoid the consequences of liver failure and cerebral oedema. Cerebral oedema and liver failure do not always have parallel evolutions. The timing of auxiliary liver transplantation should therefore, as for

OLT, be performed as quickly as possible once the patient fulfils the criteria for transplantation. The use of APOLT is controversial in patients with ALF because the graft is smaller and technical difficulties can be anticipated as compared with conventional transplantation [16]. In particular, there has been concern about the presence of a parenchymal cut surface, complex vascular anastomoses and the 'toxic effect of the remnant liver'. Another potential disadvantage is that the native liver may become cirrhotic and negate the long-term benefits of ALT, as it requires permanent immunosuppression to maintain auxiliary graft tolerance and introduces the risk of malignancy in the cirrhotic liver. When these patients survive with a cirrhotic remnant liver it can be better to remove the native liver. Patients with psychiatric history and poor compliance with previous medication can be considered for this procedure.

Because patients with APOLT are at increased risk, this procedure should only be indicated in patients aged <40 years, without evidence of chronic liver disease and without haemodynamic instability (as this has been shown to be improved by total hepatectomy of the native liver). In addition, because the amount of hepatocytes provided with this technique is lower than could be anticipated using the standard technique, only ABO-compatible, non-steatotic grafts harvested from young donors with normal liver function tests should be used.

It is somewhat paradoxical that auxiliary liver transplantations, initially advocated to avoid hepatectomy in the recipient, have proved successful when associated with a partial resection of the native liver, an operation that would have been thought 'formidable' some years ago, as patients with fulminant or subfulminant liver failure are particularly sensitive to haemodynamic variations and have disastrous haemostasis. This evolution is the result of considerable improvements in both liver resection and graft reduction. Orthotopic partial auxiliary grafts have to date predominantly been performed in patients with fulminant liver failure but have also been successful in patients with Crigler-Najjar syndrome type I [19]. This concept may also prove useful in the future in the management of liver-based inborn errors of metabolism that do not structurally damage the liver, such as homozygous familial hypercholesterolaemia, urea cycle defects, disorders of fatty acid metabolism and haemophilia [20, 21].

## Conclusions

Improvements of surgical techniques make it possible to use partial liver grafts for auxiliary transplantation with results comparable to those of conventional transplantation, at least in patients with acute liver failure but no failure of organs or systems other than the liver. Because complete regeneration of the native liver occurs in >50% of patients, who can be withdrawn from immunosuppression, the advantages of auxiliary transplantation seem to balance favourably with the potential inconvenience of this technique in selected patients.

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